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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/718,308	11/20/2000	Lakshmi Rambhatla	093/002	3507

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EXAMINER

TON, THAIAN N

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 12/05/2001

4

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/718,308

Applicant(s)

RAMBHATLA ET AL.

Examiner

Thaia N. Ton

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-33 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 29-33 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Applicants' Amendment, filed 11/1/01, Paper No. 3, has been entered.

Claims 1-28 have been cancelled.

Claims 29-33 are pending and under current examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuri-Harcuch *et al.* (US Pat. No. 5,030,105, published 6/9/1991, Reference No. A) as evidenced by EP 0953 633 A1 (Reference No. N), Hayashi *et al.* (**Mol. Pathology**, 1999, 52(1), pp. 19-24) and Alberts *et al.* (**Mol Bio of the Cell**, 1989, pp. 66 and 85).

The claims are directed to a cell population that can be cultured *in vitro*, wherein at least 60% of the cells in the population have at least three (claim 29), five (claim 31) or seven (claim 32) of the following characteristics: antibody detectable expression of AAT, antibody detectable expression of albumin, absence of antibody detectable expression of α -fetoprotein, RT-PCR detectable expression of asialoglycoprotein receptor, evidence of glycogen storage, evidence of cytochrome p450 activity, evidence of glucose6-phosphatase active and the morphological features of hepatocytes, wherein the cells with said characteristics are progeny of an established human embryonic stem cell line.

Note that claims 29-32 are product-by-process and that where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In *re Best*, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, any which shares phenotypic similarities to those set forth in claims 29-32 would anticipate the claims, even if found naturally in nature. As such, the hepatocytes as taught by Kuri-Harcuch meet the limitations of the claims (i.e., that at least 60% of the cells in the population have at least three (claim 29), five (claim 31) or seven (claim 32)).

Kuri-Harcuch *et al.* teach the culturing of hepatocytes (see Example 1, col. 4). Kuri-Harcuch *et al.* teach that these hepatocytes have the morphological features of hepatocytes (see Example 4, col. 5) and there was evidence of cytochrome p450 activity (see Example 6, col. 6). The EP 0953 633 A1 publication provides evidence for the absence of α -fetoprotein and the presence of albumin in hepatocyte cultures (see p. 23, Table 1), and Hayashi *et al.* provide evidence of genes that are expressed almost exclusively in the hepatocytes, such as albumin and AAT (see p. 19-20, bridging paragraph), and as such, it would be inherent that the absence or presence of these proteins could be detected by antibody expression. Alberts *et al.* provide evidence for

the evidence of glycogen storage and glucose-6-phosphatase activity in liver cells. Figure 2-20 (p. 66) shows the role of glucose-6-phosphate in glycolysis, and Figure 2-42 (p. 85) diagrams the liver's role in glycolysis. Furthermore, Figure 7-12 (p. 347) shows glycogen storage in liver cells.

Accordingly, Kuri-Harcuch *et al.* anticipate claims 29-32.

Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Thomson *et al.* (**Science** 282, pp. 1145-1147, 1998).

Claim 30 is directed to a cell population that comprises undifferentiated cells from a line of human embryonic stem cells. Note that claim 30 is a product-by-process claim, and therefore, a teaching of the same product obtained by a different method serves as anticipatory art against the instant claim.

Thomson *et al.* teach human embryonic stem cell lines, which remain undifferentiated (see Abstract and p. 1146, 1st column, 1st paragraph).

Accordingly, Thomson *et al.* anticipate claim 30.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29, 31 and 32, as written are confusing and indefinite. It is not clear how a ~60% of a single population of cells can have at least three and five of the described characteristics, as well as ~80% of the same cell population can have at least seven of those characteristics. The claims are independent claims and should be written as such. Clarification and/or amendment is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 29-33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kuri-Harcuch *et al.* (US Pat. No. 5,030,105, published 6/9/1991, Reference No. A) when taken with Bodnar *et al.* (**Science**, Vol. 279, 16 Jan 1998, pp. 349-352).

The claims are directed to the cell population with that can be cultured *in vitro*, wherein at least 60% of the cells in the population have at least three (claim 29), five (claim 31) or seven (claim 32) of the following characteristics: antibody detectable expression of AAT, antibody detectable expression of albumin, absence of antibody detectable expression of α -fetoprotein, RT-PCR detectable expression of asialoglycoprotein receptor, evidence of glycogen storage, evidence of cytochrome p450 activity, evidence of glucose6-phosphatase active and the morphological features of hepatocytes, wherein the cells with said characteristics are progeny of an established human embryonic stem cell line. In further embodiments, the claims are directed to the

Art Unit: 1632

described cell population, which has been genetically altered to express telomerase at an elevated level. Note that claim 33 is a product-by-process claim therefore, a teaching of the same product obtained by a different method serves as anticipatory art against the instant claim.

Kuri-Harcuch *et al.* teach a cell population of cultured hepatocytes. Kuri-Harcuch *et al.* teach that these hepatocytes have the morphological features of hepatocytes (see Example 4, col. 5) and there was evidence of cytochrome p450 activity (see Example 6, col. 6). However, Kuri-Harcuch *et al.* differ from the claimed invention in that they do not teach or suggest the genetic alteration of the cell population such that it would express telomerase at an elevated level. However, prior to the time of filing, Bodnar *et al.* teach that two human cell types (epithelial cells and fibroblasts) were transfected with vectors encoding the human telomerase catalytic subunit. Bodnar *et al.* report that these cells, in contrast to the control clones, divided vigorously and exceeded their normal lifespan by at least 20 doublings (see Abstract).

Accordingly, in view of the teachings of Bodnar *et al.*, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to transfect the hepatocyte cultures of Kuri-Harcuch *et al.* with a vector encoding the human telomerase catalytic subunit with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification, as it was art-recognized that normal human diploid cells that are cultured have a finite proliferative life-span, and thus, by maintaining human cells in culture for a longer period of time would have important applications in research and medicine (as asserted by Bodner, *Abstract* and p. 349, 1st column, 1st paragraph).

Art Unit: 1632

Thus the claimed invention as a whole was clearly *prima facie* obvious at the time the claimed invention was made especially in the absence of sufficient, clear and convincing evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Karen Hauda, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-6608. Any administrative or procedural questions should be directed to Patsy Zimmerman, Patent Analyst, at (703) 305-2758. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1632.

TNT

Thaian N. Ton
Patent Examiner
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